

METASTATIC LOBULAR CARCINOMA OF THE BREAST IN A CERVICAL-VAGINAL SMEAR

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ABSTRACT: *Metastatic carcinomas of genital or extragenital origins are unusual in cervicovaginal smears and may mimic primary neoplasms. The most common primary sites are the ovary, large bowel, stomach, breast, and kidney. The differential diagnosis between primary and metastatic carcinoma in the cervicovaginal smear may be a challenge. Cytologic examination of a cervicovaginal smear from a 48-year-old woman revealed a metastatic carcinoma. She had a combined type breast cancer two years earlier. Cytologic findings were correlated with the histology of the primary tumor. The main findings were single or "indian files" distribution of malignant cells with round, hyperchromatic nuclei. The cytologic features along with the clinical history, should alert cytopathologists to the possibility of metastatic breast cancer. Otherwise, metastatic malignant cells may mimic a primary carcinoma or carcinoma in situ.*

Key Words: Lobular Carcinoma, Breast, Cervicovaginal Smear, Metastasis.

INTRODUCTION

Metastatic carcinomas of the cervix are uncommon, with more than 50% metastasizing from the ovary and fallopian tubes. Other primary sites include the gastrointestinal tract, breast, pancreas, lung and bladder (1, 2). Metastatic neoplasms may simulate clinically and pathologically a primary cervical carcinoma (3). However, a metastatic carcinoma is an unusual diagnosis in cervicovaginal smears. The distinction of metastatic carcinoma from primary cervical malignancies is a challenge (1, 2).

Metastases of mammary carcinomas are frequently encountered in cytological materials, including pleural fluids, ascitic fluids, cerebrospinal fluids and pericardial fluids (3). Metastatic cancer is commonly diagnosed at

autopsy or in patients with known primary malignancy (1).

Histologic recognition of breast carcinoma in the cervicovaginal smear is an important finding to determine the nature of further investigation (2).

CASE REPORT

A 48-year-old woman had a diagnosis of combined type mammary carcinoma (invasive ductal and lobular carcinoma) in an excision biopsy taken from the left breast two years earlier. The malignant cells showed grade three cytology. Immunohistochemically, the cells were estrogen negative in contrast to progesterone receptor and the c-erbB 2 protein positivity. All 13 dissected lymph nodes in axillary dissection

specimen contained tumor tissue. The patient was treated with one course of radiotherapy for six weeks and then with chemotherapy.

After one year of follow up a control cervicovaginal smear was suspicious of atypical cells. The synchronous endometrial biopsy showed the presence of metastatic lobular carcinoma of the breast. A total abdominal hysterectomy and bilateral salpingoophorectomy was performed. Pathologic evaluation of the uterus confirmed the presence of metastatic carcinoma in the cervix, endometrium and right fallopian tube.

The cervicovaginal smear was prepared from a cytobrush, fixed with 95% alcohol and stained by the Papanicolaou method. The endometrial biopsy was fixed in 10% formalin and embedded in paraffin. Routine sections were stained with H&E for histopathological evaluation. Additional sections were used for histochemical and immunohistochemical staining. The avidine-biotin peroxidase method was performed using the primary monoclonal antibodies against estrogen receptor (ER) (1:50, Dako, M 7047), progesteron receptor (PR) (1:50, Dako, A 0098), carcinoembryonic antigen (CEA) (1:50, Dako, M 7072) and cytokeratin (1:50, Dako, M 0821). Appropriate positive controls were also labelled with the primary antibodies.

The background of the smear was dirty and contained benign squamous and endocervical cells. In addition malignant epithelial cells were

scattered throughout the smear. Malignant cells were larger than benign endocervical cells. The nuclei were round, hyperchromatic and demonstrated finely granular chromatin with scanty cytoplasm. Few cells contained small nucleoli. The malignant cells were distributed either singly or in groups including "indian files" (Fig. 1a and 1b).

The synchronous endometrial biopsy showed infiltrative malignant tumor of cytologic features similar to those observed in the excisional biopsy of the breast. The malignant cells showed either solid pattern or occasionally an "indian file" pattern. Cytologically, tumor cells had a high nuclear/cytoplasmic ratio and hyperchromatic nuclei. Many cells contained intracytoplasmic lumina and vacuolization (Fig. 2a and 2b). Malignant cells showed mucicarmen positivity. In addition; progesterone, cytokeratin and CEA immunoreactivity were positive in the tumor cells.

DISCUSSION

Primary cervical malignancies and metastatic cancer may show similar cytologic features, thus the distinction between both entities is important to determine patient management and prognosis. Metastatic carcinoma to the cervix is uncommon. Kumar and Hart (2) described 63 cases of extragenital cancers metastatic to the uterine corpus. However, Pomerance et al (4) reported that 54% of the adenocarcinomas of the cervix were metastatic in origin.

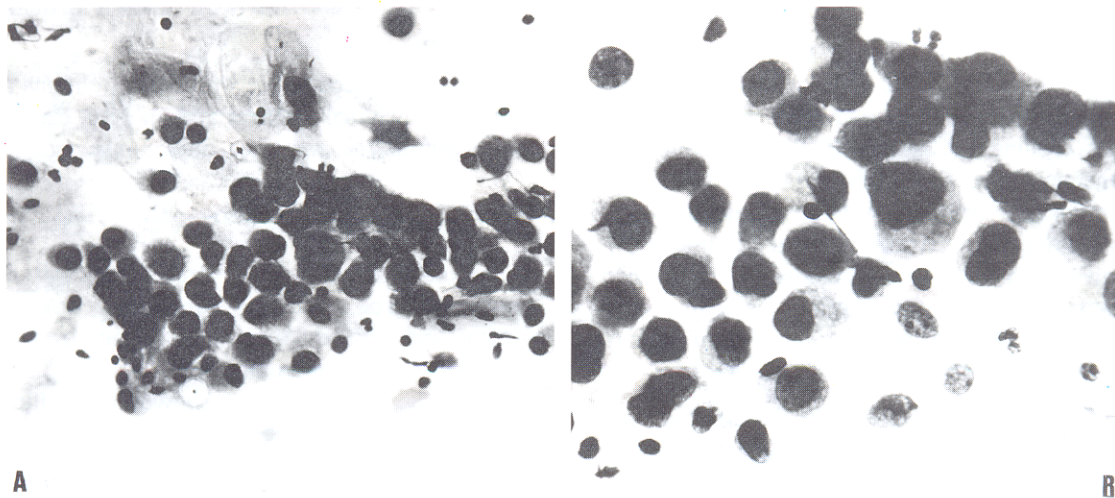


Fig. 1: A) Cervicovaginal smear: The malignant cells in clusters and singly (Papanicolaou, X 200). B) Malignant cells of lobular carcinoma of the breast. Cervicovaginal smear (Papanicolaou stain, X 400).

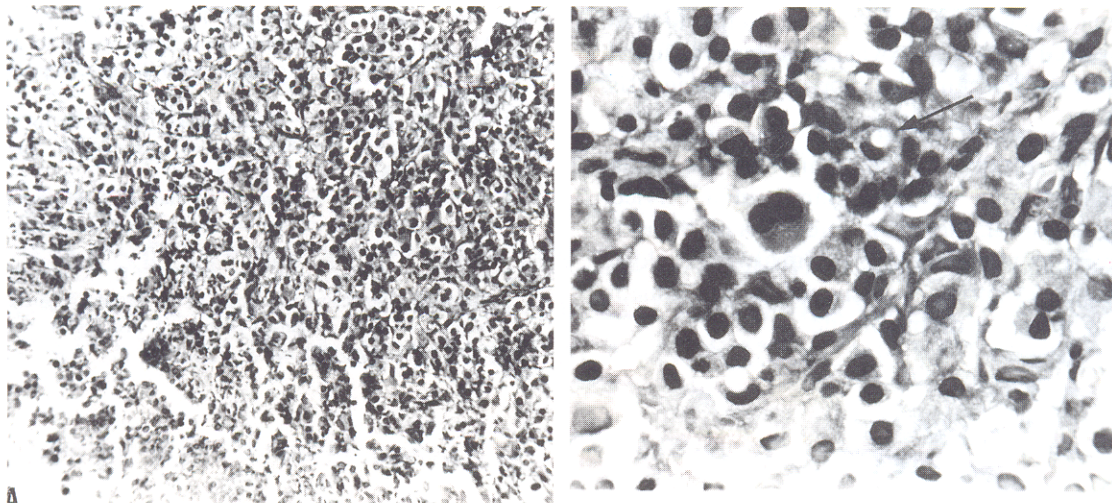


Fig. 2: A) Endometrial biopsy showing metastatic lobular carcinoma of the breast (Hematoxylin and eosin, X 40). B) Endometrial biopsy showing mammary lobular carcinoma cells with intracytoplasmic lumina* (black arrow) and vacuolization (Hematoxylin and eosin, X 200).

The most common primary sites are the ovary and fallopian tube. The remaining sites are gastrointestinal tract, breast, pancreas, lung, bladder, gallbladder and appendix (5,6). Rarely, malignant cells in the cervicovaginal smears may be the first manifestations of metastases of extragenital malignancies (7). Sometimes the metastatic carcinoma to the cervix may be clinically asymptomatic or may present as a primary gynecologic malignancy. These malignancies are usually diagnosed by endometrial biopsy or cytologically on cervicovaginal smears (8).

Breast carcinoma is the fourth most common of the carcinomas metastasizing to the cervix (3). There were cases with endometrial and cervical involvement which were initial manifestations of breast cancer (9). The most common gynecologic symptom in patients with breast cancer metastasizing to the cervix is abnormal uterine bleeding. In the present report, metastatic lobular carcinoma of the breast was detected during control smear with no clinical symptoms.

A dirty background in a cervicovaginal sample consisting of granular debris and inflammatory cells may suggest a metastatic lesion. In addition, the malignant cells may be scattered or three-dimensional groups may also be seen (1). The tumor cells are usually larger than benign endocervical cells. They show a high

nuclear/cytoplasmic ratio with hyperchromatic nuclei, finely nuclear chromatin and irregular nuclear membranes. The cytoplasm is scanty and contains occasional intracytoplasmic vacuoles (1, 2). The most common and difficult problem in differential diagnosis is the distinction of these cells from high grade squamous intraepithelial lesions and cervical adenocarcinomas. This problem may also arise from the differential diagnosis of an adenocarcinoma metastasizing from other primary sites such as stomach, pancreas, colon and ovary (1,10). Metastatic signet ring carcinoma of the breast or gastrointestinal tract may also cause considerable difficulties in differential diagnosis where other features and clinical history are important (11,12).

In the present case the cytologic features and distribution pattern of tumor cells resembled the cells of lobular carcinoma. The background of the smear was dirty and contained benign squamous and endocervical cells. In addition malignant epithelial cells were scattered throughout the smear. Malignant cells were larger than benign endocervical cells. The nuclei were round, hyperchromatic and demonstrated finely granular chromatin with scanty cytoplasm. Few cells contained small nucleoli. The malignant cells were distributed either singly or in groups including "indian files". In the synchronous endometrial biopsy diffuse infiltrative tumor

tissue containing neoplastic cells, similar to those observed in the cervicovaginal smear was found. The clinical history also supported our diagnosis.

To conclude, metastasis of lobular carcinoma to the cervix is uncommon and the initial diagnosis may be given rarely in a cervicovaginal smear. Metastatic carcinoma of breast to the cervix may present as a primary gynecologic malignancy (primary carcinoma or carcinoma in situ) or may be asymptomatic.

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